Complete Summary

GUIDELINE TITLE

Breast irradiation in women with early stage invasive breast cancer following breast conserving surgery.

BIBLIOGRAPHIC SOURCE(S)

Cancer Care Ontario Practice Guideline Initiative (CCOPGI). Breast irradiation in women with early stage invasive breast cancer following breast conserving surgery [full report]. Toronto (ON): CCOPGI; 2002 Jan [online update]. Various p. (Practice guideline report; no. 1-2). [61 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Breast Cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Oncology
Radiation Oncology
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To make recommendations about the use of breast irradiation in women with early stage invasive breast cancer following breast conservation surgery.

TARGET POPULATION

Women with early stage invasive breast cancer who have undergone breast conservation surgery

INTERVENTIONS AND PRACTICES CONSIDERED

Postoperative breast irradiation, by the following fractionation schedules:

- 50 Gy in 25 fractions to the whole breast
- 40 Gy in 16 fractions to the whole breast with a local boost to the primary site of 12.5 Gy in five fractions
- 54 Gy in 27 fractions to the whole breast
- 50 Gy in 25 fractions to the whole breast plus a boost to the tumor bed of 10 Gy in 5 fractions

MAJOR OUTCOMES CONSIDERED

Local control is the primary endpoint of interest. Survival, quality of life (addressed through the adverse effects of radiotherapy) and cosmetic outcome are also considered.

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

MEDLINE and CANCERLIT searches were completed for the years 1966 to January 1996. Search terms included: breast neoplasms, segmental mastectomy, lumpectomy, breast conservation, radiotherapy, irradiation, clinical trials, research design, practice guidelines and meta-analysis. Bibliographies from recent published reviews were reviewed and relevant articles were retrieved.

Prior to publication of the March 1997 guideline report in the August 1997 issue of Cancer Prevention & Control, these literature searches were updated and new evidence was incorporated into the published guideline.

NUMBER OF SOURCE DOCUMENTS

51 source documents

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

March 1997 Guideline

There have been four randomized trials of breast irradiation following breast conserving surgery in women with early-stage disease. These studies have consistently demonstrated a reduction in the risk of local breast recurrence ranging from 73 to 89%. In these studies, there has been no survival impact from the use of breast irradiation. The impact of breast irradiation on quality of life has not been well studied, but reported major adverse effects of breast irradiation have occurred very infrequently, and the majority of patients report a good or excellent cosmetic outcome. In discussion, the group felt that despite the failure to demonstrate a difference in survival between radiated and non-radiated patients, breast irradiation should be offered to women post-lumpectomy to reduce the risk of local breast recurrence. This was felt to be an important outcome resulting in an increase in breast conservation and avoidance of potential psychological upset associated with a recurrence.

The optimal fractionation schedule for breast irradiation has not been established. Indirect comparisons between studies suggest that several commonly used schedules are comparable. Several randomized clinical trials comparing currently used fractionation schedules are in progress. Patient participation in these studies should be encouraged. In discussion, the group felt that outside a clinical trial, patients should be treated with radiation schedules that have proven to be effective in reducing local recurrence with minimal toxicity. Consideration was given to several schedules. Two schedules with established efficacy following lumpectomy which have been used widely in Ontario were suggested: 5000 cGy in 25 fractions to the whole breast or 4000 cGy in 16 fractions to the whole breast

with a local boost to the primary site of 1250 cGy in five fractions. Shorter schedules, e.g., 4400 cGy in 16 fractions or 4000 cGy in 16 fractions have also been used routinely in some centres and there are no randomized trials that demonstrate inferior efficacy of such schedules. Further evidence regarding the use of shorter radiation schedules should be forthcoming from ongoing clinical trials.

No randomized trials directly comparing different intervals of commencing radiation post surgery were identified. Of the randomized trials considered in theour review, the maximum interval between surgery and the commencement of radiation was 12 weeks in the Ontario Clinical Oncology Group (OCOG) node-negative trial. In discussion, the group felt that the greatest weight should be put on the results of this study because it was based on patients recruited from theirour own Ontario centres.

With respect to sequencing of breast irradiation and adjuvant chemotherapy in patients eligible for this treatment, only one published randomized trial was identified. The group felt little weight could be placed on case series because of the concern of selection bias, confounders and small numbers. It was recommended that until further data become available, adjuvant chemotherapy (when appropriate) should be instituted as soon as possible following surgery. Breast irradiation should be initiated following completion of chemotherapy. Concurrent chemotherapy and radiation should be avoided when using anthracycline-containing regimens in view of the potential for increased acute and late toxicity.

A group of patients at low risk for local breast recurrence who might be spared breast irradiation cannot be identified at present but clinical trials evaluating the role of Tamoxifen are ongoing.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey consisting of nine questions asking for comments on the quality of the evidence-based recommendation (EBR), and whether the recommendation should serve as a practice guideline. Written comments were invited. Follow-up reminders were sent

at four weeks (telephone) and six weeks (mail). Results were reviewed by the Breast Cancer DSG.

The Coordinating Committee of the Cancer Care Ontario Practice Guidelines Initiative externally evaluated the practice guideline for final approval.

This practice guideline was also reviewed by two external reviewers prior to publication in the journal Cancer Prevention and Control.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse: The guideline developer released new information online January 2002. The original recommendations, released March 1997 and recorded below, currently remain unchanged.

- Women with early stage (stages I and II) breast cancer who have undergone breast conservation surgery should be offered postoperative breast irradiation.
- The optimal fractionation schedule for breast irradiation has not been established and the role of boost irradiation is unclear. Outside of a clinical trial, two commonly used fractionation schedules are suggested: 50 Gy in 25 fractions to the whole breast, or 40 Gy in 16 fractions to the whole breast with a local boost to the primary site of 12.5 Gy in five fractions. Shorter schedules (e.g., 40 or 44 Gy in 16 fractions) have also been used routinely in some centres. The enrolment of patients in ongoing clinical trials is encouraged.
- Women who have undergone breast conservation surgery should receive local breast irradiation as soon as possible following wound healing. A safe interval between surgery and the start of radiotherapy is unknown, but it is reasonable to start breast irradiation within 12 weeks of definitive surgery.
- For women who are candidates for chemotherapy, the optimal sequencing of chemotherapy and radiotherapy is unknown. It is reasonable to start radiotherapy after the completion of chemotherapy, or concurrently if anthracycline-containing regimens are not used.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

There are four randomized controlled trials and one meta-analysis comparing breast irradiation with no breast irradiation following breast conservation surgery. Evidence from six randomized trials comparing breast conservation surgery plus breast irradiation with mastectomy are also included, as well as several retrospective studies.

Evidence update: The literature search was updated and new evidence was incorporated into the published guideline in August 1997. The new evidence, from one randomized trial examining the efficacy of breast irradiation following breast conserving surgery and from a meta-analysis and randomized trial examining its adverse effects, is consistent with the data used to inform the original guideline report. The recommendations in the original report remain unchanged.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

All of the randomized trials showed a significant decrease in local recurrence rates for patients receiving radiotherapy. In the three trials with a median follow-up of five years or longer, the relative risk reduction with breast irradiation ranged from 73 to 89%. The absolute differences ranged from 16% ($p<0.001$) to 29% ($p<0.0001$). Despite the effect on local recurrence, no difference in survival was detected in any of the trials. Most of the patients with breast recurrence in these trials underwent mastectomy.

POTENTIAL HARMS

Major adverse effects of breast irradiation occur very infrequently.

- Skin erythema and fatigue were common short-term side effects of radiation therapy. Mild and moderate long-term side-effects of radiation consisting of breast edema, fibrosis, telangiectasia, and pain or discomfort were noted in 5 to 15 percent of patients treated with breast irradiation following lumpectomy.
- Two meta-analyses have suggested that adjuvant radiation after mastectomy may result in increased late cardiac mortality. This effect appears most evident for studies of older radiotherapy techniques utilizing orthovoltage or involved irradiation of the internal mammary nodes resulting in a large volume of the heart being irradiated. Increased cardiac mortality has not been demonstrated in randomized trials of breast irradiation alone.

Subgroups Most Likely to be Harmed:

Increased incidence rates of acute and late toxic effects of breast irradiation have been reported in several case reports and series of patients with scleroderma and lupus erythematosis.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

1. The association between breast irradiation and contralateral breast cancer remains unclear.
2. A group of patients at low risk for local recurrence of breast cancer who might be spared breast irradiation cannot be identified at present, but clinical trials evaluating the role of tamoxifen are underway.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Cancer Care Ontario Practice Guideline Initiative (CCOPGI). Breast irradiation in women with early stage invasive breast cancer following breast conserving surgery [full report]. Toronto (ON): CCOPGI; 2002 Jan [online update]. Various p. (Practice guideline report; no. 1-2). [61 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1997 Mar 11 (new information released online January 2002)

GUIDELINE DEVELOPER(S)

Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health.

SOURCE(S) OF FUNDING

Cancer Care Ontario, Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Provincial Breast Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

The Breast Cancer Disease Site Group is comprised of medical oncologists, radiation oncologists, surgeons, epidemiologists, pathologists and a medical sociologist. Community representatives did not participate in the development of this guideline but will in future updates.

Names of Group Members: Dr. M. Levine, Co-Chair, Medical Oncologist; Dr. K. Pritchard, Co-Chair, Medical Oncologist; Dr. D. Dhaliwal, Medical Oncologist; Dr. N. Down, Surgeon; Dr. S. Fine, Medical Oncologist; Dr. D. Ginsburg, Medical Oncologist; Dr. I. Graham, Medical Sociologist; Dr. W. Hanna, Pathologist; Dr. E. Holowaty, Director of Ontario Cancer Registry; Dr. B. Lada, Radiation Oncologist; Dr. E. Laukkanen, Radiation Oncologist; Dr. D. McCready, Surgical Oncologist; Dr. D. Mirsky, Surgeon; Dr. R. Myers, Medical Oncologist; Dr. S.E. O'Brien, Surgeon; Dr. F. Perera, Radiation Oncologist; Dr. C. Sawka, Medical Oncologist; Dr. W. Shelley, Radiation Oncologist; Dr. E. Tomiak, Medical Oncologist; Dr. D. Warr, Medical Oncologist; Dr. T. Whelan, Radiation Oncologist

Disease Site Group Staff: M. Johnston; T. Newman

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Breast Cancer Disease Site Group disclosed potential conflict of interest information.

GUIDELINE STATUS

This guideline is in the process of being rewritten and follows a January 2002 evidence update.

The original guideline was released in March 1997 and was updated with an Evidence Update Bulletin dated April 1997. The document published in August 1997 in the journal Cancer Prevention and Control incorporated the new evidence.

The guideline developer instituted a new format for their guidelines and evidence summaries: A SUMMARY of the original Practice Guideline or Evidence Summary, integrated with the most current information, replaces the ABSTRACT, RECOMMENDATION, BRIEF REPORT and EVIDENCE UPDATE.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Breast irradiation in women with early stage invasive breast cancer following breast conserving surgery. Summary. Toronto (ON): Cancer Care Ontario (CCO), 1997 Mar 11 (updated online 2002 Jan).

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on January 5, 1999. The information was verified by the guideline developer as of February 22, 1999. This summary was updated by ECRI on April 12, 2002.

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